

## Fatal Case of *Salmonella enterica* subsp. *arizonae* Gastroenteritis in an Infant with Microcephaly

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***Salmonella enterica* subsp. *arizonae* is a common gut inhabitant of reptiles, with snakes as the most common reservoir. Though human cases due to this organism are exceedingly rare, it may infect young infants and immunocompromised individuals with a history of intimate associations with reptiles. Gastroenteritis is the most common presentation; others include peritonitis, pleuritis, osteomyelitis, meningitis, and bacteremia. We report a fatal case of *S. enterica* subsp. *arizonae* gastroenteritis in a 3-month-old child with microcephaly, with a review of earlier cases and problems encountered in identification of this rare human pathogen.**

### CASE REPORT

A 3-month-old female child presented to the Emergency Unit at Ram Manohar Lohia Hospital, New Delhi, India, with a history of fever and cough for 20 days and diarrhea with mucus and blood for 15 days. There was no history of similar illness in other family members or in the community. On admission, the child, who had microcephaly, appeared highly irritable and had tachypnea and bilateral crepitations. The spleen and liver were just palpable, and there was a rash all over the body. The patient was diagnosed as having pneumonia with persistent diarrhea. A fecal sample was sent for routine culture and microscopic examination, and the patient was empirically started on broad-spectrum antibiotics (ampicillin, cefotaxime, and amikacin). Investigations revealed a hemoglobin level of 11.0 g%, a total leucocyte count of 11,500/ml, and an erythrocyte sedimentation rate of 100. A urine culture was sterile, and cerebrospinal fluid biochemistry and cytology showed no abnormality. The chest X ray showed infiltration in both lungs, while the skull X ray was normal.

The routine microscopic examination of feces did not reveal the presence of any protozoan or helminth. While fecal cultures grew a non-lactose-fermenting motile organism, the routine biochemical tests (indole, triple-sugar iron agar, citrate, urea, mannitol, and motility) for this isolate were obfuscating. The isolate was subjected to antimicrobial susceptibility testing by the Kirby-Bauer disk diffusion method and was found sensitive to furazolidone (Furoxane), ciprofloxacin, ofloxacin, ceftriaxone, and piperacillin-tazobactam. However, it revealed resistance to chloramphenicol, tetracycline, nalidixic acid, and gentamicin. Extended biotyping eventually identified the isolate as *Salmonella enterica* subsp. *arizonae*. This was further confirmed by the rapid API identification kit (Bio-Murelux). The isolate was also subsequently identified as a *Salmonella* species by a flagellin gene PCR-restriction fragment length polymorphism analysis using genus-specific primer pairs (R.

Chaudhry and D. S. Chandel, Abstr. Infect. Dis. Soc. Am. 39th Int. Meet., abstr. 291, 2001).

Following confirmed isolation of this organism in the fecal specimen, the patient's history was further elicited to trace the possibility of any contact with reptiles. Strikingly, our site investigations revealed that the child's father was a snake charmer, having a professional interaction with reptiles at home. Despite all efforts, the child's condition gradually worsened. Finally, the patient succumbed to this rare infection.

**Discussion.** Our report highlights a severe case of *S. enterica* subsp. *arizonae* gastroenteritis in an infant born to a family of snake charmers. To the best of our knowledge this is only the second case of isolation of *S. enterica* subsp. *arizonae* as a human pathogen in India and is probably the first reported case in the world of fatal *S. enterica* subsp. *arizonae* infection in an infant with microcephaly.

Reptiles, particularly snakes, are the natural reservoirs of *S. enterica* subsp. *arizonae* (20). This organism has also been responsible for severe outbreaks in turkeys and sheep (6). Though the organism is rare, several studies suggest that snakes and reptiles harbor it and transmit it to humans, resulting in gastroenteritis and systemic infections (12, 23). Such cases often occur in immunocompromised adults and young children (23). Most cases are in children less than 5 years of age. However, infants are at a particular risk (25). Reptiles are symptomless carriers of this pathogen and are probably infected through contaminated water, feed, or soil (25). Earlier findings indicate that these bacteria probably exist as commensal flora in the animal gut. Widespread contamination of the home environment and a significant number of cases occur due to pet reptiles (22). Often these infections are invasive and lead to complications such as meningitis, septicemia, and osteomyelitis (G. Makin, M. Abu Harb, A. Finn, and S. Partridge, Letter, Lancet 348:200, 1996).

*S. enterica* subsp. *arizonae* was first described by Caldwell and Ryerson in 1939 (5) and was named *Salmonella dar-es-salaam* (after the African city where it was first isolated). It was subsequently placed in genus *Arizona*, with a single species, *A.*

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TABLE 1. *S. enterica* subsp. *arizonae* human infections with varying clinical pictures (1952 to 2002)

Case no.	Age	Sex	Underlying disease	Exposure to reptile	Infective syndrome(s)	Outcome	Yr of report	Reference	Treatment
1	7 yr	F	Sickle cell anemia	Unknown	Otitis media	Recovered	1952	1	Unknown
2	2 yr	M	Langerhans cell histiocytosis	Unknown	Septicemia, osteomyelitis	Recovered	1953	10	Chloramphenicol
3	2.5 yr	F	Sickle cell anemia	Unknown	Osteomyelitis	Recovered	1971	15	Ampicillin, gentamicin
4	30 yr	M	None	Unknown	Bacteremia	Recovered	1976	2	Chloramphenicol
5	8 wk	F	None	Unknown	Meningitis	Recovered	1980	16	Ampicillin, chloramphenicol
6	11 yr	M	None	Pet snakes	Osteomyelitis	Recovered	1984	L <sup>a</sup>	Ampicillin
7	19 yr	F	SLE	Rattlesnake capsule	Bacteremia	Recovered	1988	25	Ampicillin
8	25 yr	M	HIV <sup>b</sup>	Rattlesnake capsule	Pleural effusion	Recovered	1988	25	Ampicillin, trimethoprim, sulfamethoxazole
9	51 yr	M	Cardiomyopathy	Rattlesnake capsule	Pleural effusion	Recovered	1988	25	None
10	15 yr	F	SLE	Rattlesnake capsule	Septicemia, sinusitis	Recovered	1991	19	Ampicillin
11	12 yr	F	Lymphocytic leukemia	Rattlesnake pills	Sepsis	Died	1991	19	Died before treatment
12	69 yr	M	Gastric cancer	Rattlesnake pills	Peritonitis	Recovered	1992	26	Cefotaxime, gentamicin
13	6 yr	M	None	Rattlesnake meat	Gastroenteritis	Recovered	1995	18	Ceftriaxone
14	11 days	M	None	Pet iguana	Gastroenteritis	Recovered	1997	22	Ampicillin, metronidazole, gentamicin
15	8 wk	M	Netherton syndrome	Pet snake	Gastroenteritis	Recovered	1997	22	Ciprofloxacin
16	7 mo	F	None	Pet iguana	Osteomyelitis	Recovered	2000	24	Ceftriaxone
17	10 yr	M	None	Snake bite	Wound infection	Recovered	2001	3	Cefuroxime
18	3 mo	F	Microcephaly	Pet reptiles	Gastroenteritis	Died	2002	This study	Ampicillin, amikacin, cefotaxime

<sup>a</sup> Croop et al., letter.  
<sup>b</sup> HIV, human immunodeficiency virus infection.

*hinshawii*, within the tribe *Salmonella* based on biochemical properties (12). The placement and nomenclature of this species have constantly remained a matter of scientific debate. However, DNA homology studies helped to reclassify it as *Salmonella enterica* subsp. *arizonae* (1983). Since its first description in 1939, it was subsequently reported in snakes (14), lizards, and turtles. It appears to be more prevalent in snakes, with as many as 78.8% harboring the organism (13). Later it was also isolated from fowl, turkeys, ducks, and mammals, such as dogs, cats, monkeys, and goats (11).

It was initially considered to be a reptile pathogen; the first report of human infection came in 1944 (J. M. Croop, B. Shapiro, G. Alpert, J. M. Campos, and W. Zavod, Letter, *Pediatr. Infect. Dis.* 3:188, 1984). Turtle-associated salmonellosis was also reported in 1963 (7). Now it is established as a well-known pathogen in young children and in patients with impaired immunity.

*S. enterica* subsp. *arizonae* is a gram-negative bacillus and a member of the *Enterobacteriaceae*. The distinguishing biochemical features include the ability to ferment lactose, utilize malonate, and liquefy gelatin and the inability to grow in the presence of KCN. As many *S. enterica* subsp. *arizonae* strains ferment lactose within 48 h, they may be routinely discarded as nonpathogens if grown from feces (28). The presence of H<sub>2</sub>S is an important diagnostic clue for routine screening (8). In the present case the isolate did not ferment lactose after 24 h of incubation (a routine test in our laboratory) but had distinguishing biochemical features.

Salmonellas are well adapted to diverse niches, capably surviving 89 days in tap water, 115 days in pond water, and over 30 months in bovine manure (21). *S. enterica* subsp. *arizonae* is no exception. Reptiles get infected by this group of organisms through soil, water, or feed. The organism can also penetrate turtle eggs (9), and transovarian passage in turtles has also been reported (17).

Human infection commonly occurs in individuals with underlying disease or immunodeficiency or in infants infected by intimate contacts with reptile pets. The most common infection is gastroenteritis (20), with 73% of illnesses occurring in the first 3 months of exposure (27). The gastroenteritis associated with *S. enterica* subsp. *arizonae* is similar to other salmonellosis. It requires an incubation of 2 to 48 h and is characterized by fever, headache, abdominal pain, vomiting, and diarrhea. Stools are expulsive, copious, and frequently mixed with blood and mucus (Croop et al., letter). There is a substantial risk of dehydration due to the severity of diarrheal illness. This was observed in this case, where the child could not sustain severe dehydration, developed shock, and eventually died of cardiorespiratory arrest.

A literature survey (Table 1) yielded 17 case reports of *S. enterica* subsp. *arizonae* infection, of which 11 were children, including 4 infants. Eleven of those 17 had an underlying disease such as AIDS, systemic lupus erythematosus (SLE), cancer, or leukemia. Clinical presentations varied: four cases each with gastroenteritis, bacteremia, and osteomyelitis; two with pleural effusion; and one each with otitis media, peritonitis, meningitis, and wound infection. Most of these strains of *S. enterica* subsp. *arizonae* were sensitive to all common antibiotics.

Another interesting fact was that this strain was unique in its

reactivity in serological tests. Though it was identified biochemically, serological tests were confusing. There was no agglutination by poly(O) antiserum. However, it reacted with poly(H) antiserum. An extensive literature survey could trace only one report of a poly(O)-inagglutinable *S. enterica* subsp. *arizonae* isolate, suggesting that the expression of mannose-resistant type III fimbriae is often associated with complete O inagglutinability (1).

A carrier state is not uncommon, and a recurrence of *S. enterica* subsp. *arizonae* sepsis in immunocompromised patients after 1 year has been reported (Croop et al., letter). In addition to gastroenteritis, complications such as bacteremia, sepsis, osteomyelitis, and meningitis have also been reported (4).

We suggest that the identification of this organism with routine biochemical tests and serological reagents may be problematic. Such cases, when presented with a suggestive history, should be handled with extra care. Molecular techniques, such as a *Salmonella*-specific PCR, may prove a valuable tool for confirming the etiology, allowing timely institution of appropriate therapy to prevent morbidity and mortality due to this rare human pathogen.

*S. enterica* subsp. *arizonae*, though an uncommon human pathogen, is a common organism in reptiles, particularly snakes. The prevalence of human infections is probably underestimated since the gastrointestinal problems they generate were considered usually benign. However, this pathogen should be considered in the differential diagnoses of patients with sepsis and severe gastroenteritis who have a history of contact with reptiles or ingestion of snake meat preparations, e.g., as powdered capsules. Young children are at a particular risk of acquiring such infections. Therefore, proper history should be obtained in such cases. Ownership of reptiles should be discouraged, especially in households with children less than 5 years of age.

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